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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/650,284	08/28/2003	Rutai Hui	043774/268252	6701

826 7590 10/13/2004

ALSTON & BIRD LLP
BANK OF AMERICA PLAZA
101 SOUTH TRYON STREET, SUITE 4000
CHARLOTTE, NC 28280-4000

EXAMINER	
GALVEZ, JAMES JASON	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 10/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/650,284	HUI ET AL.	
	Examiner	Art Unit	
	J. Jason Galvez	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) *1-10,12,13,15-19 and 22-32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11, 14, 20, and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☒ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/28/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group II in the reply filed on 9/10/2204 is acknowledged. Applicant's election has been considered an election without traverse because Applicant did not direct any arguments toward the restriction requirements posed by the Examiner.

The new claims directed to polynucleotides, claims 22-32, are not directed to the elected subject manner and are distinct for the reasons of record in the office action of 8/13/2004. Therefore, the claims under consideration for examination are as follows: the original Group II, claims 11 and 14, and the newly submitted claims 20 and 21, which are directed to elected subject matter.

The requirement is still deemed proper and is therefore made FINAL.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file. However, a translation of the foreign priority papers has not been submitted. Should applicant desire to obtain the benefit of foreign priority under 35 U.S.C. 119(a)-(d), a translation of the foreign application should be submitted under 37 CFR 1.55 in reply to this action.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (p. 27, paragraph [0124]). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Objections to the disclosure are further drawn to sequences and a lack of sequence identifies in the disclosure. Applicant is required to make appropriate changes in reference to sequences recited on pp. 4, 24, 26, 27, 29, 30, 32, and 41. The following quote from the MPEP is applicable:

2421.02 Summary of the Requirements of the Sequence Rules. Basically, the sequence rules define a set of symbols and procedures that are both mandatory and the only way that an applicant is permitted to describe information about a sequence that falls within the definitions used in the rules. Thus, 37 CFR 1.821 defines a "sequence" and a "Sequence Listing" for the purpose of the rules, the requirements for specific symbols, and formats for the "Sequence Listing," the requirement for a computer readable form (CRF) of the "Sequence Listing," and the deadlines for complying with the requirements. 37 CFR 1.822 to 37 CFR 1.824 set forth detailed descriptions of the requirements that are mandatory for the presentation of sequence data, and 37 CFR 1.825 sets forth procedures that are available to an applicant in the event that amendments to the sequence information or replacement of the computer readable copy become necessary.

The sequence rules embrace all unbranched nucleotide sequences with ten or more bases and all unbranched, non-D amino acid sequences with four or more amino acids, provided that there are at least 4 "specifically defined" nucleotides or amino acids. The rules apply to all sequences in a given application, whether claimed or not. All such sequences are relevant for the purposes of building a comprehensive database and properly assessing prior art. It is therefore essential that all sequences, whether only disclosed or also claimed, be included in the database.

The use of the trademarks: RNA GENTS, QUICK PREP, ZAP EXPRESS, cDNA GIGAPACK, BIGDYE, and ALF EXPRESS have been noted in this application.

Trademarks should be fully capitalized wherever they appear and should be

accompanied by the generic terminology. Applicant is advised to carefully review the disclosure for any other trademarks the Examiner my have over looked and in doing so Applicant should also make the appropriate corrections.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner that might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 11, 14, 20, and 21 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the isolated polypeptide disclosed as SEQ ID No. 2, does not reasonably provide enablement for SEQ ID No. 2 fragments, analogs, or derivatives and compositions with an intended use for the treatment of cardiocerebral-vascular disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The factors to be considered when determining if the disclosure satisfies the enablement requirement have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill

of those in the art, the predictability or unpredictability of the art, and the breath of claims. *Ex Parte Forman*, (230 USPQ 546 (Bd. Pat. App. & Int. 1986)) ; *In re Wands*, 858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988).

Claims 11 and 14 are drawn to "active fragment, analog or derivative" and "active fragment", respectfully. SEQ ID No. 2 fragments, analogs or derivatives are defined in the disclosure by examples that in no way limit what is being claimed (p. 7, paragraph [0036]). In addition, Applicant has stated that fragments, analogs or derivatives could encompass SEQ ID No. 2 with "residues substituted by conservative or non-conservative amino acid residues". It is well known in the art that single amino acid changes can severely affect polypeptide function. Luck et al. have reported that even conservative amino acid changes, R→K, can alter activity by as much as 90% (Molecular Endocrinology 1991, Vol. 5(12): pp. 1880-1886, esp. p. 1881, table 1). For the reasons given above and the non-limiting manner in which Applicant has defined terms in the claims it would not be possible to make and/or use the invention commensurate in scope due the quantity of experimentation necessary, the absence of an adequate number of working examples, the unpredictability of the art, and the breadth of the claims.

Claim 11 is drawn to "a polypeptide having at least 85% homology". For the reasons given above regarding single amino acid changes, it is unknown whether a polypeptide with 85% homology would work within the framework of the claimed invention. Accordingly, it would not be possible to make and/or use the invention commensurate in scope due the quantity of experimentation necessary, the absence of

an adequate number of working examples, the unpredictability of the art, and the breadth of the claims.

Claim 14 is drawn to "an effective amount of the polypeptide of claim 11". An effective amount of the claimed polypeptide is not defined in the specification or in the accompanying figures. In addition, it is unclear to the Examiner what an effective amount would do. Therefore, it would not be possible to make and/or use the invention commensurate in scope due to the absence of any working examples showing "an effective amount".

Claims 20 and 21 are drawn to a polypeptide and a pharmaceutical composition intended to treat cardiocerebral-vascular disease. The disclosure states that the claimed polypeptide is upregulated in the aorta during subacute and chronic heart failure, but there were no experiments performed where the claimed polypeptide was given to animals under conditions of cardiocerebral-vascular disease. Upregulation of a particular polypeptide does not necessarily imply a therapeutic utility of the claimed polypeptide. For example, during ischemia and reperfusion injury in the heart proinflammatory cytokines, such as IL-8, that mediate tissue injury are upregulated (Vallely et al., The J of Thoracic and Cardiovascular Surgery 2002, Vol 124(4): pp. 758-767, esp. Figure 1). In the case of IL-8 it would not be beneficial to administer more IL-8 because that would likely result in increased tissue damage. In addition, there are several reasons why polypeptide-based therapies could fail, ranging from cellular inaccessibility to immunological responses (Science 1999, Vol 286: pp. 304-306, esp. p. 304, column 2, lines 10-16). Therefore, without administering the polypeptides in any

manner it is not possible to make and/or use the invention commensurate in scope due to the quantity of experimentation necessary, the absence of working examples, and the nature of the invention.

Claims 11, 14, 20, and 21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, and any combination thereof.

Claims 11, 14, 20, and 21 are drawn to "active fragment", "analog or "derivative". The specification does not limit what is meant by "active fragment", "analog" or "derivative" and therefore does not provide any distinguishing characteristics. Since there are no distinguishing characteristics, such as structure, a person of ordinary skill in the art cannot envision the claimed genus drawn to "active fragment", "analog", or "derivative".

Claim 11 is drawn to "a polypeptide having at least 85% homology". The claim does not require that the polypeptide possess any particular biology activity or any particular conserved structure. Since there are no distinguishing characteristics, such as structure or function, a person of ordinary skill in the art cannot envision the claimed genus drawn to "a polypeptide having at least 85% homology".

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11, 14, 20, and 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 11, 14, 20, and 21 are drawn to "active fragment", "analog or "derivative". The disclosure has not defined an activity of the claimed polypeptide, without the disclosure of an activity the claim is indefinite in regards to what an "active fragment", "analogue", or "derivative" encompasses. In addition, without disclosing any essential structure it is unclear as to what constitutes an "active fragment", "analogue", or "derivative" and to what degree changes or modifications in the original molecule would result in an "active fragment", "analogue", or "derivative".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 11, 14, 20, and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Gao et al. [WO/0034474 (6/15/2000)]. Gao et al. teach a sequence, which is a vascular endothelial growth factor homologue, that is 100% identical to SEQ ID No. 2 of the present application. In addition, Gao et al. teach that the sequence claimed can be used to treat cerebral ischemia and myocardial infarction, both of which classify as cardiocerebral-vascular diseases (p. 66, lines 13-17). Thus, Gao et al. meet the limitations of the claims.

Claims 11, 14, 20, and 21 are rejected under 35 U.S.C. 102(e) as being anticipated by Gao et al. [US Patent No. 6,432,673 (Filing date: 12/07/1999)]. Gao et al. teach a sequence, which is a vascular endothelial growth factor homologue, that is 100% identical to SEQ ID No. 2 of the present application. In addition, Gao et al. teach that the sequence claimed can be used to treat cerebral ischemia and myocardial infarction, both of which classify as cardiocerebral-vascular diseases (column 38, lines 25-30). Thus, Gao et al. meet the limitations of the claims.

Conclusion

NO CLAIMS ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **J. Jason Galvez, Ph.D**. whose telephone number is **571-272-2935**. The examiner can normally be reached Monday through Friday 9 AM to 5 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Brenda Brumback, Ph.D.** can be reached at **571-272-0887**.

The fax phone number for the organization where this application or proceeding is assigned is **703-872-9306**. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

JJG
10/12/04

JANET ANDRES
PRIMARY EXAMINER